

Claims

1. A live recombinant bovine adenovirus
vector (BAV) system selected from the group consisting
5 of:

(a) a system wherein part or all of the
E1 gene region is replaced by a heterologous nucleotide
sequence encoding a foreign gene or fragment thereof;

(b) a system wherein a part or all of the
10 E3 gene region is replaced by a heterologous nucleotide
sequence encoding a foreign gene or fragment thereof; and

(c) a system wherein part or all of the
E1 gene region and part or all of the E3 gene region are
deleted and a heterologous nucleotide sequence encoding a
15 foreign gene or fragment thereof is inserted into at
least one of the deletions.

2. The BAV system of claim 1 which is a
bovine adenovirus type 3.

3. The BAV system of claim 1 wherein (a) a
recombinant BAV wherein part or all of the E1 gene region
is replaced by a heterologous nucleotide sequence
encoding a foreign gene or fragment thereof.

4. The BAV system of claim 1 wherein (b) a
recombinant BAV wherein a part or all of the E3 gene
region is replaced by a heterologous nucleotide sequence
encoding a foreign gene or fragment thereof.

5. The BAV system of claim 1 wherein the
foreign nucleotide sequence is with or without the
control of an exogenous promoter.

6. The BAV system of claim 1 wherein (c) a system wherein part or all of the E1 gene region and part or all of the E3 gene region are deleted and a heterologous nucleotide sequence encoding a foreign gene or fragment thereof is inserted into at least one of the deletions.

7. A recombinant vector system comprising the entire BAV genome and a plasmid capable of generating a recombinant virus by in vivo recombination following cotransfection of a suitable cell line comprising the entire BAV genome representing the wild-type BAV genome and a plasmid comprising an adenovirus left end nucleotide sequences containing the E1A gene region or a plasmid comprising adenovirus right end sequences containing the E3 gene region, the plasmid with a heterologous nucleotide sequence encoding a foreign gene or fragment thereof substituted for part or all of the E1 and/or E3 gene regions, respectively.

8. A recombinant bovine adenovirus vector system comprising two plasmids capable of generating a recombinant virus by in vivo recombination following cotransfection of a cell line comprising

(1) a first plasmid comprising the entire BAV genome except for a deletion of part or all of the E1 and/or E3 gene regions, and

(2) a second plasmid comprising BAV left or right end nucleotide sequences containing the E1 or E3 gene regions, respectively, having a heterologous nucleotide sequence encoding a foreign gene or fragment thereof inserted for the deletion of a part or all of the E1 or E3 gene regions.

9. A live viable recombinant bovine adenovirus (BAV) comprising a deletion of part or all of the E1 gene region, a deletion of part or all of the E3 gene region or deletion of both, and inserted into at least one deletion a heterologous nucleotide sequence coding for a polypeptide or an antigenic determinant produced by a disease causing organism.

10. A live viable recombinant bovine adenovirus (BAV) for producing an immune response in a mammalian host comprising:

(1) a live bovine adenovirus (BAV) modified to contain a heterologous nucleotide sequence coding for a polypeptide or an antigenic determinant corresponding to the desired immune response in association with or without

(2) an effective promoter for said nucleotide sequence to provide expression of said antigenic determinant in immunogenic non-pathogenic quantities.

11. A live recombinant bovine adenovirus expression system comprising a deletion of all or part of the E1 gene region or all or part of the E3 gene region, or both deletions and inserted in at least one deletion a heterologous nucleotide sequence coding for a foreign gene or fragment thereof under control of an expression promoter with or without one or more polyadenylation signal.

12. A recombinant mammalian cell line comprising bovine adenovirus (BAV) E1 gene region, said recombinant cell line thereby capable of allowing replication therein of a bovine adenovirus comprising an E1 deletion which may or may not be replaced by a

heterologous or homologous nucleotide sequence encoding a foreign gene or fragment thereof.

13. The cell line of claim 12 which is a
5 bovine cell line.

14. The recombinant mammalian cell line of
claim 12 wherein the heterologous or homologous
nucleotide sequence encoding the foreign gene or fragment
10 thereof is selected from the group consisting of a bovine
adenovirus (BAV) E1 polypeptide,, a BAV E1-associated
polypeptide, a growth factor, a cellular receptor or
other cellular polypeptide.

15. A recombinant mammalian cell line
comprising bovine adenovirus E1 genes, said recombinant
cell line thereby capable of allowing DNA-mediated
transfection to generate a recombinant bovine adenovirus
(BAV) selected from the group consisting of:

20 (a) a recombinant BAV wherein part or all of
the E1 gene region is replaced by a heterologous
nucleotide sequence encoding a foreign gene or fragment
thereof,

(b) a recombinant BAV wherein part or all of
25 the E3 gene region is replaced by a heterologous
nucleotide sequence encoding a foreign gene or fragment
thereof,

(c) a recombinant BAV wherein part or all of
the E1 gene region and part or all of the E3 gene region
30 are deleted and inserted into at least one deletion a
heterologous nucleotide sequence encoding a foreign gene
or fragment thereof,

(d) a recombinant BAV wherein part or all of
the E1 gene region and/or part or all of the E3 gene
35 region are deleted and inserted into at least one

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deletion a heterologous nucleotide sequence encoding more than one foreign gene or fragment thereof to produce a recombinant fusion protein, and

5 (e) a mutant BAV wherein part or all of the E1 gene region and/or part or all of the E3 gene region are deleted.

16. A method of preparing a recombinant polypeptide or fragment thereof which comprises:

10 (1) infecting the mammalian cell line of claim 12, with a recombinant bovine adenovirus comprising a deletion of part or all of the E1 gene region and/or part or all of the E3 gene region and inserted into at least one deletion a heterologous nucleotide sequence
15 encoding the polypeptide or fragment thereof,

(2) replicating the recombinant virus in a recombinant cell line under conditions to provide for expression of the polypeptide, and

20 (3) recovering the recombinant polypeptide or antigenic fragment thereof.

17. A method of isolating a polypeptide which comprises:

25 (1) replicating a recombinant mammalian cell line of claim 12 under conditions to provide for expression of the polypeptide, and

(2) recovering the polypeptide or fragment thereof.

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18. A method for eliciting an immune response in a mammalian host to protect against an infection comprising:

administering a vaccine composition
35 comprising a live recombinant BAV of claim 1 wherein the

foreign gene or fragment encodes an antigen with or without a pharmaceutically acceptable carrier.

19. A method for eliciting an immune response
5 in a mammalian host to protect against an infection comprising:

administering a vaccine comprising a recombinant polypeptide or fragment thereof prepared by a method of claim 16 with or without a pharmaceutically
10 acceptable carrier.

20. A vaccine for protecting a mammalian host against infection comprising a live recombinant adenovirus of claim 1 wherein the foreign gene or
15 fragment encodes an antigen with or without a pharmaceutically acceptable carrier.

21. A vaccine for protecting a mammalian host against infection comprising a recombinant antigen
20 prepared by a method of claim 16 with or without a pharmaceutically acceptable carrier.

22. A mutant bovine adenovirus (BAV) comprising a deletion of part or all of E1 and/or a
25 deletion of part or all of E3.

23. A method for providing gene therapy to a mammal in need thereof to control a gene deficiency which comprises administering to said mammal a live recombinant
30 bovine adenovirus containing a foreign nucleotide sequence encoding a non-defective form of said gene under conditions wherein the recombinant virus vector genome is incorporated into said mammalian genome or is maintained independently and extrachromosomally to provide
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expression of the required gene in the target organ or tissue.

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